

Adolescent Scalp Psoriasis

Update on Topical Combination Therapy

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ABSTRACT

Plaque psoriasis can begin early in life and negatively affect quality of life. Topical agents are generally recommended as first-line therapy for plaque psoriasis. The synergy of a vitamin D analog and a steroid in a topical fixed-combination formulation provides more favorable effectiveness and tolerability as compared with either agent alone. The safety and effectiveness of a once-daily calcipotriene/betamethasone dipropionate topical suspension have been established in children 12 to 17 years of age with scalp plaque psoriasis. Combination topical formulations and once-daily dosing decrease regimen complexity and may increase adherence. Accommodation of vehicle preference may also improve adherence and real-life effectiveness. (*J Clin Aesthet Dermatol.* 2015;8(7):43–47.)

Psoriasis, a common dermatologic disorder affecting individuals of all ages, can begin early in life. Up to 35 percent of cases begin before 18 years of age, affecting 0.7 percent of children.^{1–3} This incidence doubled between 1970 and 1999 and is currently 40.8 cases per 100,000.⁴ The median age at diagnosis (10.6 years) has remained stable in the United States.⁴

It is important for clinicians to appreciate the impact of psoriasis on children and teenagers. Even mild forms of psoriasis can affect childhood psychosocial functioning and quality of life (QoL).^{2,5–7} The scalp plaques and possible associated alopecia can be particularly troublesome during adolescence and detrimental to the individual's sense of self during the transition to adulthood.^{8,9}

Topical therapy can be safe and effective in juvenile psoriasis. Topical treatments are a first-line option in adults, and some have been approved for use in adolescents (Table 1).^{10–19} This article reviews the distinguishing features of psoriasis in younger patients and the considerations that enter into the choice of treatment.

CLINICAL FEATURES

Plaque psoriasis (psoriasis vulgaris) is the most common form of juvenile psoriasis, affecting nearly 75 percent of children and adolescents with psoriasis.⁴ The pattern of presentation in juvenile psoriasis can vary from the presentation in adults.⁴ In juvenile plaque psoriasis, the plaques are typically localized to the scalp, postauricular

region, elbows, and knees.^{20,21} The plaques are erythematous, with a silvery scale that is finer than in adult psoriatic plaques.²²

The hairline and occipital scalp are often the first site of involvement in children.^{6,21,23–25} Among juvenile plaque psoriasis patients from eight geographically diverse United States dermatology clinics, 79 percent had a history of scalp involvement.²⁶

TREATMENT STRATEGIES

Despite differences between juvenile and adult psoriasis, the therapies used are essentially the same for both. The formulations and dosage strengths are based on age, extent and severity of disease, affordability, and availability of the therapeutic agent.^{20,27}

Topical agents are generally recommended as first-line therapy for psoriasis vulgaris.²⁷ The most commonly prescribed topical agents include corticosteroids, calcipotriene with or without topical corticosteroids, medicated shampoos, and calcineurin inhibitors. Many regimens include a combination of therapies.^{20,27}

TOPICAL CORTICOSTEROIDS

For patients with psoriasis who are <18 years of age, topical corticosteroids are the most commonly prescribed medication in the United States and are generally considered to be a first-line treatment for these patients.^{21,27–29} Topical corticosteroids are anti-inflammatory

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TABLE 1. Approved topical corticosteroid formulations for adolescents^{10–14,16–19}

CORTICOSTEROID	APPROVAL AGE (YEARS)
Betamethasone dipropionate 0.05% Cream Ointment Lotion	≥13
Betamethasone dipropionate 0.05% Gel	≥12
Clobetasol propionate 0.05% Cream Ointment Foam Gel and Solution	≥12
Halobetasol 0.05% Cream Ointment	≥12

and anti-proliferative, reducing pruritus, scale, and erythema.²⁵ Topical corticosteroids have been approved for the treatment of corticosteroid-responsive dermatoses in adolescents (Table 1), but they lack specific labeling for pediatric psoriasis.^{10–14,16–19}

Children have higher absorption of topical agents due to a higher capacity for skin penetration and higher skin-surface-area-to-body-weight ratio, making them more vulnerable than adults to local and systemic adverse events (AEs).³⁰ Therefore, high-potency topical corticosteroid use in children should be carefully monitored.³⁰

TOPICAL VITAMIN D ANALOGS

The topical vitamin D analogs calcipotriene (a synthetic form of vitamin D₃, sometimes referred to as calcipotriol) and calcitriol (1,25-dihydroxyvitamin D₃) stimulate differentiation and inhibit proliferation of keratinocytes.^{8,21,27,31} After corticosteroids, calcipotriene is the most frequently prescribed topical medication for juvenile psoriasis.²⁹ Calcipotriene was FDA-approved for psoriasis in adults in 1993.^{32,33} Studies have reported clearance or significant clinical improvement of mild-to-moderate psoriasis vulgaris in children and adolescents treated with calcipotriene.^{34–39} No significant change in serum calcium level or vitamin D levels and no consistent or clinically important changes in biochemical parameters have been reported after calcipotriene treatment.^{34–37,39}

TOPICAL CORTICOSTEROID AND VITAMIN D ANALOG COMBINATION THERAPY

The combination of a topical corticosteroid and a vitamin D₃ analog has been recommended as the treatment of

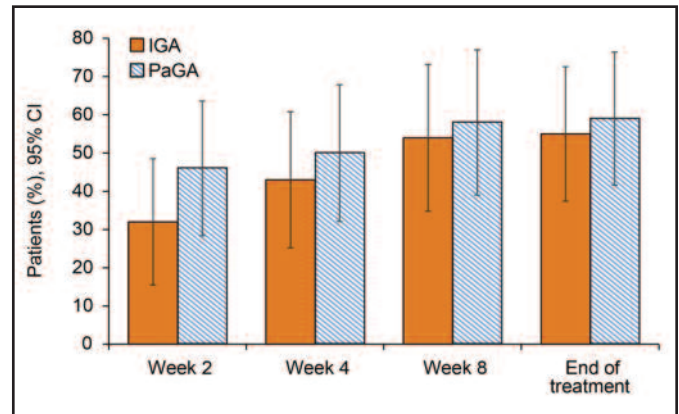


Figure 1. Proportion of patients experiencing treatment success as determined by investigator and patient global assessments in an open-label, non-controlled, 8-week trial of the effect of calcipotriene plus betamethasone topical suspension on HPA axis and calcium metabolism in adolescents with extensive scalp psoriasis conducted in the US.⁴⁵ Values are percent \pm 95% confidence intervals. Treatment consisted of once-daily calcipotriol 50 μ g/g plus betamethasone dipropionate 0.5mg/g. Week 8 data include only observed cases at that time point; end-of-treatment data include the last value recorded for that parameter. Investigator's Global Assessment score: clear, almost clear, mild, moderate, severe, very severe; Patient's Global Assessment score: clear, very mild, mild, moderate, severe. Treatment success: Investigator's Global Assessment of clear or almost clear; Patient's Global Assessment of clear or very mild. Adapted with permission from Eichenfield LF, et al. *Pediatr Dermatol.* 2015;32(1):28–35.⁴⁵

choice for psoriasis.^{21,30,40–42} Although topical vitamin D analogs may be used as monotherapies, they are usually applied with topical steroids, for their steroid-sparing effects. The complementary action makes the combination more efficacious than either agent used alone, reduces the required dosage of corticosteroid, and minimizes the potential for AEs.^{40,43}

In 2014, calcipotriene/betamethasone dipropionate topical suspension (0.005%/0.064%) received United States Food and Drug Administration (FDA) approval for the topical treatment of plaque psoriasis of the scalp in patients 12 to 17 years of age.¹⁵ The safety and effectiveness of the once-daily topical suspension were established in two uncontrolled, prospective, eight-week clinical trials in subjects aged 12 to 17 years of age with plaque psoriasis of the scalp, one conducted in the United States and the other being a multinational study conducted in Canada, France, and the United Kingdom.^{15,44,45} In the US trial, treatment success rated according to the Investigator's Global Assessment (IGA) (clear or almost clear on a scale of clear, almost clear, mild, moderate, severe, very severe) and the Patient's Global Assessment (PaGA) (clear or very mild on a scale of clear, very mild, mild, moderate, severe) was achieved by 55 and 58 percent of patients at the end of

treatment, respectively (Figure 1).⁴⁵ Higher rates of treatment success (85% IGA, 87% PaGA) were reported in the multinational trial at the end of treatment.⁴⁴

No serious AEs were reported in either trial. Seventy percent of AEs (14/16) in the US trial⁴⁵ and 52 percent (33/64) in the multinational trial were mild.⁴⁴ The most common AEs (occurring in $\geq 4\%$ of patients) were cough (n=3), oropharyngeal pain (n=3), nasopharyngitis (n=2), and upper respiratory tract infection (n=2) in the US trial⁴⁵ and headache (n=4), pharyngitis (n=4), upper respiratory tract infection (n=4), and decreased urine calcium (n=3) in the multinational trial.⁴⁴ One case of adrenal suppression, as indicated by a 30-minute post-stimulation cortisol level ≤ 18 $\mu\text{g/dL}$, was the only adverse drug reaction in the US trial, and it occurred without clinical manifestation.⁴⁵ After discontinuation of study medication and an adreno-corticotrophic hormone (ACTH) challenge test four weeks later, cortisol levels were normal. In the multinational trial, seven adverse drug reactions were reported.⁴⁴ Acne, blood parathyroid hormone increase, and urine calcium decrease were moderate in severity, while the others were mild. No hypercalcemia or clinically relevant changes in markers of calcium metabolism or in any other biochemistry or hematology parameters were reported in either the multinational trial (Figure 2) or the US trial.^{44,45}

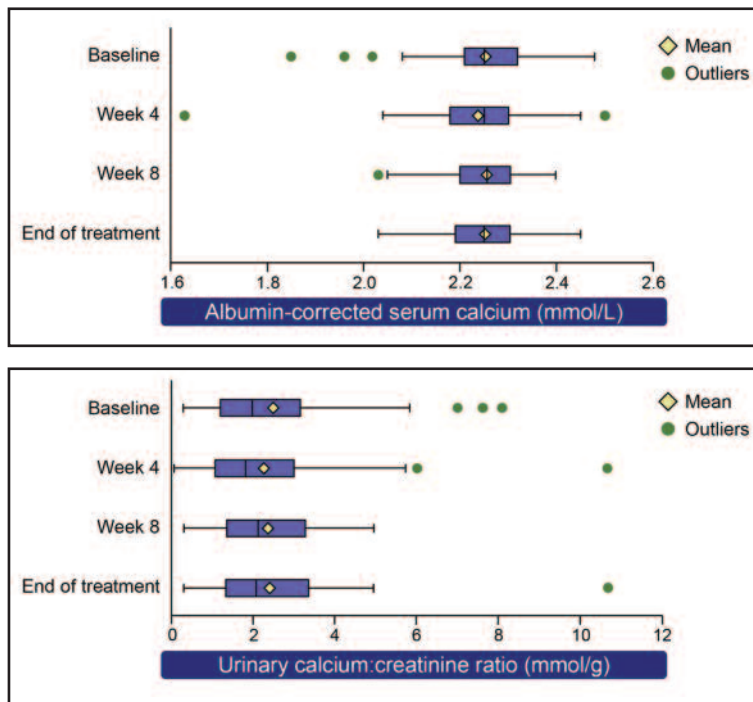


Figure 2. Mean changes with two-sided 95% confidence intervals in calcium metabolism from baseline to end of treatment.⁴⁴

Adapted with permission from Gooderham M, et al. *Br J Dermatol.* 2014;171:1470–1477.⁴⁴

PATIENT ADHERENCE CONSIDERATIONS

Nonadherence to medication is a well-acknowledged challenge to treatment effectiveness in psoriasis and other chronic dermatologic diseases,^{46–48} even in clinical trials. Among adults enrolled in a psoriasis clinical trial (N=30) in which medication use was monitored for eight weeks, overall patient adherence rates declined from 85 percent at Week 1 to 51 percent at Week 8.⁴⁹ In a study of children ≤ 12 years of age with atopic dermatitis, adherence from baseline to the end of the study was only 32 percent.⁵⁰

REGIMEN COMPLEXITY

Adherence may be related to the complexity and perceived convenience of the treatment regimen.⁵¹ Although topical regimens for psoriasis, such as vitamin D analogs and corticosteroids, are safe and effective, applying them as individual monotherapies involves complicated treatment directions that may reduce adherence, especially during long-term treatment. Combination formulations of topical medications decrease the complexity of the regimen and may increase adherence and responsiveness to treatment.^{52,53}

Adherence to treatment with calcipotriene/betamethasone dipropionate topical suspension was assessed in a single-arm study of adolescents 12 to 17 years of age with moderate-to-severe scalp psoriasis.⁴⁴ Fifty-nine percent of the patients were fully or at least >90 percent adherent in the eight-week study. The once-daily dosing of calcipotriene/betamethasone dipropionate topical

suspension may further promote adherence.⁵⁴ Adherence to once-daily therapy in a 12-week study of adults with psoriasis was nearly double the adherence to twice-daily therapy (82.3% vs. 44.0%, $P < 0.001$).⁵⁵

VEHICLE PREFERENCE

Cosmetic and tactile properties (the “look” and “feel”) of topical formulations also influence adherence.⁴³ The PRO-long study (Patient-Reported Outcomes in a long-term study) is the first long-term study of patients’ experiences with once-daily formulations of the fixed-combination calcipotriene/betamethasone in real-life clinical practice over 52 weeks.⁵⁶ Recently published interim data from PRO-long suggested that patients found the suspension formulation to be more convenient, easier to use, and faster to apply than the ointment.

Adolescents often object to applying greasy ointments to their body.^{21,25} Patients who find their topical therapy unacceptably greasy and messy to use, especially on hair-bearing areas, may be less likely to adhere to the treatment regimen.^{43,57} The current consensus is that most patients prefer the calcipotriene/betamethasone dipropionate suspension because it is less greasy and less likely to stick to clothing than a comparable once-daily ointment.⁵⁸

SUMMARY

Psoriasis is a chronic dermatologic disorder that can begin in childhood or adolescence. Topical therapy is the

mainstay of treatment in adolescents as well as in adults. Although the majority of adolescent cases of psoriasis are considered mild, the psychosocial effects of psoriasis in children and adolescents can be profound. Effective treatment can help to mitigate some of these effects.

Advances in therapy have improved the outlook for treating juvenile psoriasis. Topical vitamin D analogs and corticosteroids are established first-line treatments for psoriasis, with consideration of some safety concerns. Combination topical agents offer beneficial clinical characteristics while providing a favorable tolerability profile. Calcipotriene/betamethasone dipropionate topical suspension was recently approved in the United States for the treatment of plaque psoriasis of the scalp in patients 12 to 17 years of age. Clinical studies have shown this combination topical suspension to be a well-tolerated and effective once-daily treatment regimen in adolescents.

Simplifying the treatment regimen and improving vehicle acceptability may increase treatment adherence and real-life effectiveness in adolescent patients.

REFERENCES

- Augustin M, Glaeske G, Radtke MA, et al. Epidemiology and comorbidity of psoriasis in children. *Br J Dermatol*. 2010;162:633–636.
- de Jager ME, de Jong EM, van de Kerkhof PC, et al. An inpatient comparison of quality of life in psoriasis in childhood and adulthood. *J Eur Acad Dermatol Venereol*. 2011;25:828–831.
- Raychaudhuri SP, Gross J. A comparative study of pediatric onset psoriasis with adult onset psoriasis. *Pediatr Dermatol*. 2000;17:174–178.
- Tollefson MM, Crowson CS, McEvoy MT, Maradit KH. Incidence of psoriasis in children: a population-based study. *J Am Acad Dermatol*. 2010; 62:979–987.
- Beattie PE, Lewis-Jones MS. A comparative study of impairment of quality of life in children with skin disease and children with other chronic childhood diseases. *Br J Dermatol*. 2006;155:145–151.
- Fotiadou C, Lazaridou E, Ioannides D. Management of psoriasis in adolescence. *Adolesc Health Med Ther*. 2014;5:25–34.
- de Jager ME, de Jong EM, Evers AW, van de Kerkhof PC, Seyger MM. The burden of childhood psoriasis. *Pediatr Dermatol*. 2011;28:736–737.
- Benoit S, Hamm H. Childhood psoriasis. *Clin Dermatol*. 2007;25:555–562.
- Fox FE, Rumsey N, Morris M. “Ur skin is the thing that everyone sees and you cant change it!”: exploring the appearance-related concerns of young people with psoriasis. *Dev Neurorehabil*. 2007;10:133–141.
- Betamethasone Dipropionate Cream [package insert]. Lincoln, NC: Actavis Mid Atlantic LLC; 2006.
- Betamethasone Dipropionate Gel [package insert]. Melville, NY: E. Fougera & Co.; 2000.
- Clobetasol Propionate Cream and Ointment [package insert]. Baltimore, MD: Alphapharm USPD Inc.; 2000.
- Diprolene® Lotion [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2014.
- Diprolene® Ointment [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2014.
- Taclonex® Topical Suspension [package insert]. Parsippany, NJ: LEO Pharma Inc.; 2014.
- Temovate® Gel [package insert]. Research Triangle Park, NC: Glaxo Wellcome Inc; 2000.
- Temovate® Scalp Application [package insert]. Research Triangle Park, NC: Glaxo Wellcome Inc; 2000.
- Ultravate® [package insert]. Jacksonville, FL: Ranbaxy Laboratories Inc.; 2012.
- Olux® [package insert]. Newton, PA: Prestium Pharma, Inc.; 2014.
- Silverberg NB. Pediatric psoriasis: an update. *Ther Clin Risk Manag*. 2009;5:849–856.
- Bhutani T, Kamangar F, Cordoro KM. Management of pediatric psoriasis. *Pediatr Ann*. 2012;41:e1–e7.
- Morris A, Rogers M, Fischer G, Williams K. Childhood psoriasis: a clinical review of 1262 cases. *Pediatr Dermatol*. 2001;18:188–198.
- Howard R, Tsuchiya A. Adult skin disease in the pediatric patient. *Dermatol Clin*. 1998;16:593–608.
- Busch AL, Landau JM, Moody MN, Goldberg LH. Pediatric psoriasis. *Skin Therapy Lett*. 2012;17:5–7.
- Tollefson MM. Diagnosis and management of psoriasis in children. *Pediatr Clin North Am*. 2014;61:261–277.
- Mercy K, Kwasny M, Cordoro KM, et al. Clinical manifestations of pediatric psoriasis: results of a multicenter study in the United States. *Pediatr Dermatol*. 2013;30:424–428.
- Shah KN. Diagnosis and treatment of pediatric psoriasis: current and future. *Am J Clin Dermatol*. 2013;14:195–213.
- Lara-Corrales I, Xi N, Pope E. Childhood psoriasis treatment: evidence published over the last 5 years. *Rev Recent Clin Trials*. 2011;6:36–43.
- Vogel SA, Yentzer B, Davis SA, Feldman SR, Cordoro KM. Trends in pediatric psoriasis outpatient health care delivery in the United States. *Arch Dermatol*. 2012;148:66–71.
- Herz G, Blum G, Yawalkar S. Halobetasol propionate cream by day and halobetasol propionate ointment at night for the treatment of pediatric patients with chronic, localized plaque psoriasis and atopic dermatitis. *J Am Acad Dermatol*. 1991;25:1166–1169.
- Charakida A, Dadzie O, Teixeira F, et al. Calcipotriol/betamethasone dipropionate for the treatment of psoriasis. *Expert Opin Pharmacother*. 2006;7:597–606.
- Dovonex® Fe [package insert]. Rockaway, NJ: Warner Chilcott (US), Inc.; 2007.
- Dovonex. Drugs@FDA. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist. Accessed September 29, 2014.
- Park SB, Suh DH, Youn JI. A pilot study to assess the safety and efficacy of topical calcipotriol treatment in childhood psoriasis. *Pediatr Dermatol*. 1999;16:321–325.
- Perez A, Chen TC, Turner A, Holick MF. Pilot study of topical calcitriol (1,25-dihydroxyvitamin D₃) for treating psoriasis in children. *Arch Dermatol*. 1995;131:961–962.
- Oranje AP, Marcoux D, Svensson A, et al. Topical

- calcipotriol in childhood psoriasis. *J Am Acad Dermatol*. 1997;36:203–208.
37. Darley CR, Cunliffe WJ, Green CM, et al. Safety and efficacy of calcipotriol ointment (Dovonex) in treating children with psoriasis vulgaris. *Br J Dermatol*. 1996;135:390–393.
38. Patrizi A, Neri I, Rizzoli L, Varotti C. Topical calcipotriol in childhood psoriasis. *Acta Derm Venereol*. 1999;79:477.
39. Saggese G, Federico G, Battini R. Topical application of 1,25-dihydroxyvitamin D₃ (calcitriol) is an effective and reliable therapy to cure skin lesions in psoriatic children. *Eur J Pediatr*. 1993;152:389–392.
40. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. *J Am Acad Dermatol*. 2009;60:643–659.
41. de Jager ME, de Jong EM, van de Kerkhof PC, Seyger MM. Efficacy and safety of treatments for childhood psoriasis: a systematic literature review. *J Am Acad Dermatol*. 2010;62:1013–1030.
42. van de Kerkhof PC, Hoffmann V, Anstey A, et al. A new scalp formulation of calcipotriol plus betamethasone dipropionate compared with each of its active ingredients in the same vehicle for the treatment of scalp psoriasis: a randomized, double-blind, controlled trial. *Br J Dermatol*. 2009;160:170–176.
43. Menter A, Gold LS, Bukhalo M, et al. Calcipotriene plus betamethasone dipropionate topical suspension for the treatment of mild to moderate psoriasis vulgaris on the body: a randomized, double-blind, vehicle-controlled trial. *J Drugs Dermatol*. 2013;12:92–98.
44. Gooderham M, Debarre JM, Keddy-Grant J, et al. Safety and efficacy of calcipotriol plus betamethasone dipropionate gel in the treatment of scalp psoriasis in adolescents 12–17 years of age. *Br J Dermatol*. 2014;171:1470–1477.
45. Eichenfield LF, Ganslandt C, Kurvits M, Schlessinger J. Safety and efficacy of calcipotriene plus betamethasone dipropionate topical suspension in the treatment of extensive scalp psoriasis in adolescents ages 12 to 17 years. *Pediatr Dermatol*. 2015;32(1):28–35.
46. Storm A, Andersen SE, Benfeldt E, Serup J. One in 3 prescriptions are never redeemed: primary nonadherence in an outpatient clinic. *J Am Acad Dermatol*. 2008;59:27–33.
47. Zschocke I, Mrowietz U, Karakasili E, Reich K. Non-adherence and measures to improve adherence in the topical treatment of psoriasis. *J Eur Acad Dermatol Venereol*. 2014;28(Suppl 2):4–9.
48. Serup J, Lindblad AK, Maroti M, et al. To follow or not to follow dermatological treatment—a review of the literature. *Acta Derm Venereol*. 2006;86:193–197.
49. Carroll CL, Feldman SR, Camacho FT, Manuel JC, Balkrishnan R. Adherence to topical therapy decreases during the course of an 8-week psoriasis clinical trial: commonly used methods of measuring adherence to topical therapy overestimate actual use. *J Am Acad Dermatol*. 2004;51:212–216.
50. Krejci-Manwaring J, Tusa MG, Carroll C, et al. Stealth monitoring of adherence to topical medication: adherence is very poor in children with atopic dermatitis. *J Am Acad Dermatol*. 2007;56:211–216.
51. Shepherd J, Taheri A, Feldman SR. Once-daily topical treatment for psoriasis: calcipotriene + betamethasone two-compound topical formulation. *Clin Cosmet Investig Dermatol*. 2013;7:19–22.
52. Yentzer BA, Ade RA, Fountain JM, et al. Simplifying regimens promotes greater adherence and outcomes with topical acne medications: a randomized controlled trial. *Cutis*. 2010;86:103–108.
53. Koehler AM, Maibach HI. Electronic monitoring in medication adherence measurement. Implications for dermatology. *Am J Clin Dermatol*. 2001;2:7–12.
54. McCormack PL. Calcipotriol/betamethasone dipropionate: a review of its use in the treatment of psoriasis vulgaris of the trunk, limbs and scalp. *Drugs*. 2011;71:709–730.
55. Zaghloul SS, Goodfield MJ. Objective assessment of compliance with psoriasis treatment. *Arch Dermatol*. 2004;140:408–414.
56. Lambert J, Hol CW, Vink J. Real-life effectiveness of once-daily calcipotriol and betamethasone dipropionate gel vs. ointment formulations in psoriasis vulgaris: 4- and 12-week interim results from the PRO-long study. *J Eur Acad Dermatol Venereol*. 2014;28:1723–1731.
57. Augustin M, Holland B, Dartsch D, et al. Adherence in the treatment of psoriasis: a systematic review. *Dermatology*. 2011;222:363–374.
58. Dauden E, Bewley A, Lambert J, et al. Expert recommendations: the use of the fixed combination calcipotriol and betamethasone dipropionate gel for the topical treatment of psoriasis. *J Eur Acad Dermatol Venereol*. 2014;28(Suppl 2):22–32. ●